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Malignant Transformation of Fibrous Dysplasia

A Case Report and Review of the Literature

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A 34-year-old man developed a spindle-cell sarcoma originating in a preexisting lesion of monostotic fibrous dysplasia. A review of the literature reveals 83 cases of a malignant degeneration in fibrous dysplasia; osteosarcoma was the most common type of tumor. The next most common were fibrosarcoma and chondrosarcoma. The malignant tumor usually developed in the third or fourth decade of life. The most frequent anatomic sites were the craniofacial bones, the femur, and the tibia. Twenty-three of the 83 cases were treated with local radiation. In fibrous dysplasia, any abrupt alteration in the clinical course, manifested by pain and swelling, raises the possibility of malignant degeneration.

The term *fibrous dysplasia* was introduced by Lichtenstein and Jaffe[48,50] to describe a group of bone lesions with histologic and clinical features that distinguish them from other fibroosseous lesions. Some of the cases they described had solitary (monostotic) lesions, some had multiple (polyostotic) lesions, and some were associated with multiple bone lesions, precocious puberty, and skin pigmentation (Albright's syndrome).[3]

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Fibrous dysplasia is one of several bone diseases known to undergo malignant change. (Others are Paget's disease,[31,72] enchondromatosis (Ollier's disease),[51,72] and solitary and multiple osteochondromas.[29,72]) A malignant tumor can also develop in relation to a bone infarct[28,53] or an osteomyelitis sinus[2,26] or can occur as a result of irradiation.[5,6,8,15,19,24,33,37,38,63,64]

The purpose of this article is to report a case of malignant transformation of fibrous dysplasia and to review the literature on this subject.

CASE REPORT

A 34-year-old man presented with a two-year history of pain and swelling of the left leg. Roentgenographic examination (Fig. 1) revealed an osteolytic lesion involving the lower third of the shaft of the tibia, eroding and expanding the cortex; above the lesion the cortical bone of the tibia was irregularly thickened and sclerotic. A bone scan showed increased uptake in the region of the lesion. Routine blood chemistry studies gave normal values.

At the age of five years the patient had been treated at another institution for a lesion involving the same tibia. The lesion had been biopsied, and a diagnosis of fibrous dysplasia had been made. Review of the original histologic sections showed the characteristic changes of fibrous dysplasia (Fig. 2). The lesion consisted of mature fibrous tissue containing trabeculae of nonlamellar bone, some of which were arranged in the curved plates typical of fibrous dysplasia.

At this stage (age, 34 years) biopsy study of the lytic lesion showed a malignant spindle-celled sarcoma, without evidence of any recognizable

FIG. 1. Anteroposterior (AP) and lateral roentgenograms, showing the osteolytic lesion involving the lower part of the shaft of the tibia. The cortical bone above the lesion is thickened and sclerotic.

FIG. 2. Biopsy at age five, showing characteristic changes of fibrous dysplasia (original magnification, ×92).

pattern of histologic differentiation (Fig. 3). The tumor tissue consisted of interweaving bundles of elongated cells; numerous mitoses were present, some of them abnormal.

A below-knee amputation was performed. The amputation specimen showed a mass of hemorrhagic fleshy tissue, 6 × 5.5 cm, expanding the lower tibia (Fig. 4). The cortical bone is thinned and deficient anteriorly. Proximal to the tumor, the tibial cortex is thickened and dense. A roentgenogram of the specimen showed this abnormal bone to have a coarsely trabecular appearance and an irregular endosteal margin (Fig. 5).

Histologically, the tumor tissue in the amputation specimen showed the same appearance as in the biopsy specimen. Much of the tissue is cystic and hemorrhagic. Sections from the dense cortical bone showed thickened bone trabeculae together with fibrous tissue containing collections of foamy histiocytic cells (Fig. 6).

The histologic structure of the abnormal bone in the amputation specimen suggested that the authors were dealing with the end stage of the evolution of the original fibrous dysplasia lesion. They concluded that the spindle-celled sarcoma originated in the tissue of the long-standing fibrous dysplasia lesion.

Follow-up data showed that the patient died, with pulmonary metastases, two years after amputation.

DISCUSSION

Malignant transformation of fibrous dysplasia is a rare but established complication

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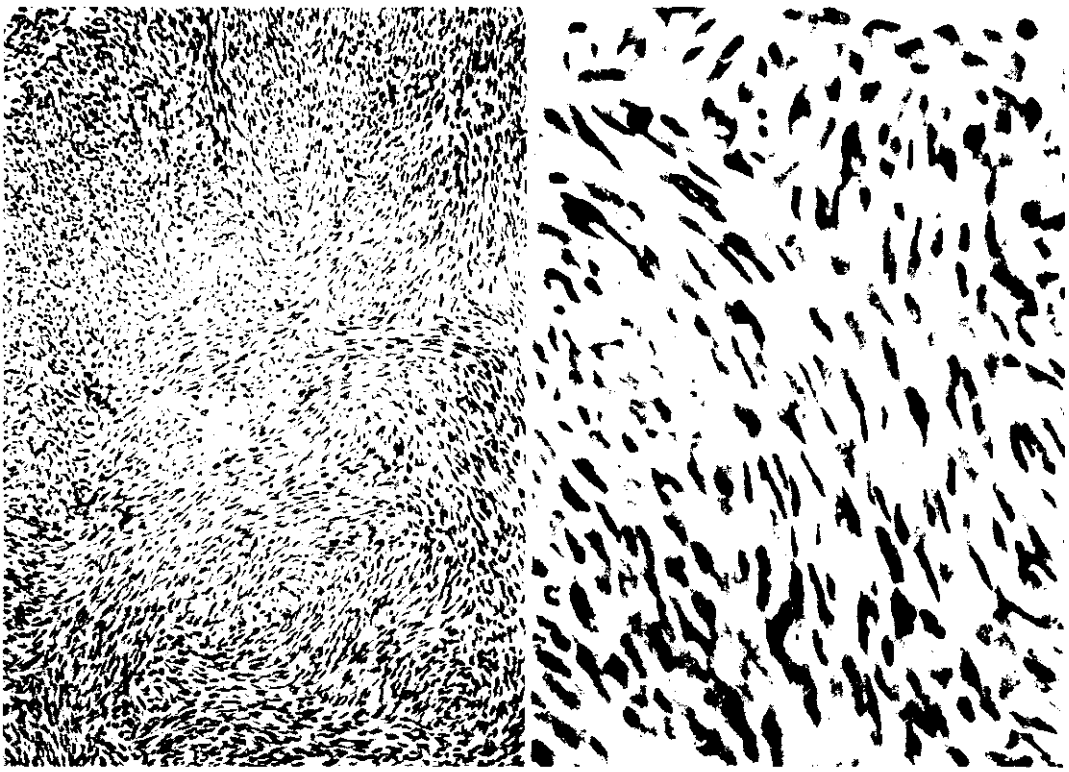
FIG. 2. Biopsy at age five, showing characteristic changes of fibrous dysplasia (original magnification, ×92).

of this disease. The first well-documented account is that of Coley and Stewart, in 1945,[18] although it is clear that cases had been encountered by earlier workers.[60] Many case reports have now been published. From the 53 papers available,[1,4,7,9–14,16–18,20,23,25,27,30,32–36,39–47,49,52,54–59,61,62,65–68,70–75] the authors collected data, not always complete, from 83 cases, with reference to the age and sex of the patient, the anatomic site and type (monostotic or polyostotic) of the lesion, the histologic type of the malignant tumor, the use of radiation treatment for the original lesion, and the period of survival after the diagnosis of the malignant tumor. The results are shown in Table 1.

In most reported cases, the diagnosis of fibrous dysplasia was made in childhood but



FIGS. 3A AND 3B. (A) Biopsy at age 34, showing an undifferentiated malignant spindle-celled tumor (original magnification, ×147). (B) Biopsy at age 34. Numerous mitotic cells are apparent (original magnification ×587).

the malignant tumor developed during the third or fourth decades of life. It has been estimated that only about 0.4% of all cases of fibrous dysplasia undergo malignant change, although a higher incidence (approximately 4%) was found in cases of Albright's syndrome.[65] Among the cases reviewed, men and women were equally affected. Of the 72 cases with information available, 41 had monostotic fibrous dysplasia and 31 had the polyostotic form. A variety of types of tumor were encountered. Osteosarcoma was the most frequent histologic type (40 cases), followed by fibrosarcoma (22 cases) and chondrosarcoma (11 cases). The craniofacial region, particularly the mandible and maxilla, was the most common site of involvement (27 cases), followed by the femur (20 cases), tibia (9 cases), and pelvis (8 cases). This distribution appears to correspond to the relative frequency of occurrence of fibrous dysplasia in different parts of the skeleton.

In 23 cases, local radiation was mentioned as a mode of treatment for the original fibrous dysplasia lesion. In 46 cases it was stated that there had been no antecedent radiotherapy, and there was no mention of such treatment in the remaining 14 cases. It is clear that radiation is not a prerequisite for malignant transformation in fibrous dysplasia. The authors believe that the tumors in the 23 cases treated with radiation should be

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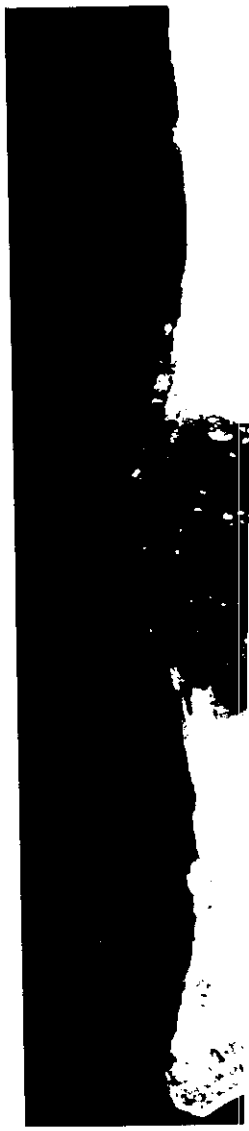

FIG. 4. Amputatio
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regarded as radiation-induced sarcomas not necessarily related to fibrous dysplasia.

Prognosis for sarcomas developing in fibrous dysplasia is poor. Most patients died with pulmonary metastases, and the mean survival period was 3.4 years. Patients with fibrous dysplasia should remain under medical supervision, unless the lesions have been surgically eradicated in their entirety. The late development of pain and swelling, particularly in an older patient, should alert the

FIG. 4. Amputation specimen hemorrhagic tumor of the tibia. Note the thickened cortical bone proximal to the lesion.

FIG. 5. Roentgenogram of a sawn slab of tissue from the surface of the specimen in Figure 4.

TABLE 1. Malignant Transformation of Fibrous Dysplasia: Data from Reported Cases

Histologic Diagnosis	Number of Cases	Age (Years) Mean Range	Sex		Type of Lesion		Site		Radiation Treatment		Mean Survival (Years)
Osteosarcoma	40	29.7	M	17	P	16	Facial bones	18	Rad	15	2.4
		3–54	F	16	M	22	Femur	12	No	20	
			U	7	U	2	Tibia	7	U	5	
							Fibula	1			
							Humerus	1			
							Scapula	1			
							Rib	1			
							Ilium	1			
Fibrosarcoma (and spindle-cell sarcoma)	22	38.1	M	8	P	4	Facial bones	7	Rad	6	2.4
		15–61	F	7	M	11	Skull	1	No	10	
			U	7	U	7	Femur	4	U	6	
							Tibia	1			
							Humerus	1			
							Rib	2			
							Ischium	1			
Chondrosarcoma	11	34.0	M	4	P	6	Femur	1	Rad	1	4.3
		11–51	F	5	M	3	Humerus	1	No	7	
			U	2	U	2	Ilium	3	U	3	
							Ischium	1			
							Metatarsal	1			
Other	10	33.6	M	4	P	5	Mandible	2	Rad	1	5.5
		17–49	F	6	M	5	Femur	2	No	9	
							Tibia	1			
							Scapula	2			
							Ilium	1			
							Pubis	2			
							Shoulder	1			
Total	83	32.7	M	33	P	31	Facial bones	27	Rad	23	3.0
		3–61	F	34	M	41	Skull	1	No	46	
			U	16	U	11	Femur	20	U	14	
							Tibia	9			
							Fibula	1			
							Humerus	3			
							Scapula	3			
							Rib	3			
							Ilium	5			
							Ischium	2			
							Pubis	1			
							Metatarsal	1			
							Shoulder	1			

M, male; F, female; P, polyostotic; M, monostotic; Rad, radiation; No, no radiation; U, unknown.

physician to the possibility of malignant change, the presence of which can be established by radiologic examination and biopsy study. Because of the risk of radiation sarcoma, radiotherapy should not be used in the treatment of fibrous dysplasia.

FIG. 6. Appearance of thickened cortical bone seen in Figures 4 and 5 (original magnification, ×92).

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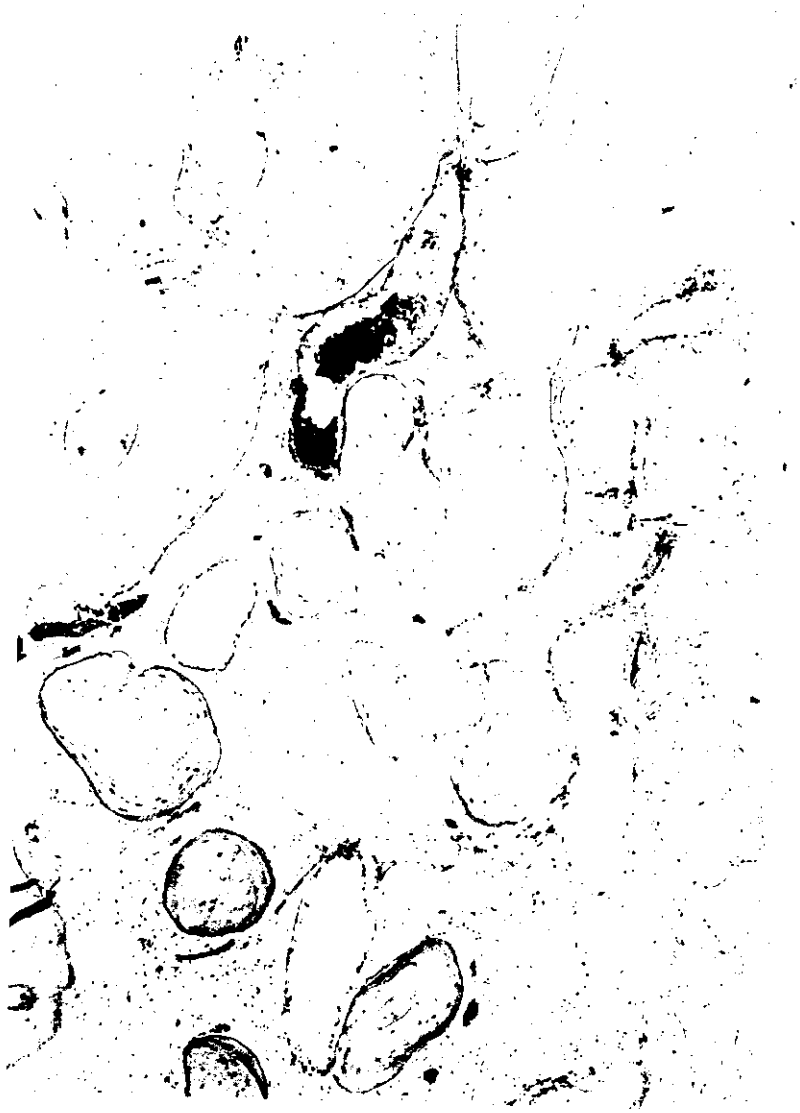

FIG. 6. Appearance of thickened cortical bone seen in Figures 4 and 5 (original magnification, ×92).

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